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EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/20/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/295,663	Joshi et al.
Examiner	**Art Unit**
Joseph Woitach	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 25, 2003* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *38-44, 47-50, and 69-87* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *38-44, 47-50, and 69-87* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This application, filed April 21, 1999, claims benefit to provisional applications: 60/082,665 filed April 22, 1998, 60/111,635 filed December 9, 1998, and 60/11,637 filed December 9, 1998.

Applicants' amendment filed March 25, 2003, paper number 26, has been received and entered. The specification has been amended. Claims 52-54 have been canceled. Claims 38, 69 and 74 have been amended. Claims 38-44, 47-50 and 69-87 are pending and currently under examination.

Response to Amendment

The declaration of Dr. Ian MacLachlan filed under 37 CFR 1.132 filed March 25, 2003, attached to paper number 26, is insufficient to overcome the rejection of claims 38-44, 47-51 and 69-87 based upon the rejection made under 35 USC 102 and 35 USC 103 as set forth in the last Office action. The declaration will be discussed in detail below as it pertains to the specific rejections.

Claim Objections

Claim 42 stands objected to because "GDEPT" is the acronym which is not specifically defined in the specification or the art of record. When not specifically defined in the

specification, the first presentation of an abbreviated term should be denoted by setting forth the full name indicating the term to be used subsequently. It is noted that the specification has been amended, however this amended passage does not specifically define the abbreviated term but rather provides a first presentation of the acronyms. While the claims are read in light of the specification, the metes and bounds of the claims should be defined within the recitation of the claim and be interpreted and stand by themselves. In this case because the specification does not specifically define the abbreviations as encompassing any specific term, the first presentation of the abbreviated term in the claim should be denoted by setting forth the full name indicating the term to be used subsequently.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-44, 47, 48 and 69-87 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a methods of introducing a nucleic acid encoding a foreign gene and of inhibiting the growth of cancer cells comprising the steps of: (a) first, administering a cell cycle blocking agent; and (b) second, administering a nucleic acid wherein the transfection efficiency is increased by at least 50%, does not reasonably provide enablement

for administering the nucleic acid before the cell cycle blocking agent wherein the transfection efficiency is increased by at least 50% is withdrawn.

Amendments to the independent claims to clearly set forth the method steps has obviated the basis of the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 38-44, 47-50, 69-73, 79-81 and 84-86 stand rejected under 35 U.S.C. 102(b) as being anticipated by Son *et al.*

Applicants summarize the requirements for anticipation under 35 USC 102 and argue that the present claims as amended are not anticipated by Son *et al.* In particular, Applicants note the transfection efficiency must be increased by at least 50%, and note that the results of Son *et al.* only demonstrate a 30% increase in efficiency (pages 6-7). Further, the specific anticancer drugs methotrexate, etoposie, cytosine arabinonucleoside, doxorubicin, and caboplatin are discussed by Son *et al.* to have no significant sensitizing effect (page 7). Finally, Applicants have provided a declaration by Dr. MacLachlan wherein Dr. MacLachlan concludes that Son et al. specific

statement does not disclose all of the specific elements encompassed by the claims, specifically increasing the efficiency by at least 50% (page 7 and declaration, section 7). See Applicants' amendment, pages 6-7. Applicants' arguments have been fully considered, but not found persuasive.

Examiner notes the requirement of the instantly claimed method to increase transfection efficiency at least 50%, however the results presented in Son *et al.* meet this limitation. Applicants indicate that the results present in Son *et al.* demonstrate an increase of only 30%, however the 30% presented in results represents a measured CAT activity as a percent conversion. Each of the percent activities should be interpreted as a factor of the control showing little or no activity. For example in figure 2, the 30% activity at day 7 represents approximately 300 fold increase over the control. This is a 300% increase, which thus anticipates the "increased by at least 50%" recited in the instant claims. Likewise, the pretreatment of the cells in culture (figure 3) and the analysis of the affects of various chemotherapeutic agents (figure 4) must be interpreted with respect to the control, not as an absolute value. This interpretation is consistent with Son *et al.* who interpret the affects of pretreatment as having "about a 2-fold more transfectability" than other samples (page 12671, top of second column describing figure 3). A two-fold increase would be a 200% increase in transfection efficiency. The passage of Son *et al.* cited by Applicants and discussed by Dr. MacLachlan is noted, and though Examiner would agree that Son *et al.* considered and summarized their specific results as having no significant affect on transfection efficiency, the specific data as provided in the graph clearly demonstrates

that the transfection efficiency was increased over 50% for vincristine as compared to the control not treated with vincristine. It may be that Son *et al.* was summarizing the absolute amount of activity which was measured and considered this to be less significant than that demonstrated by cisplatinin. What Son *et al.* contemplated in writing this passage can not be specifically ascertained, however the data presented in the graph (figure 4) clearly demonstrates the change in percent transfection efficiency over 50% for vincristine. Vincrisitne is a vinca alkaloid, thus the teachings of the methods and conditions set forth in Son *et al.* meet the limitations of the present claims. Therefore, for the reasons above and of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 38-44, 47-50, 69-73, 79-81 and 83-86 rejected under 35 U.S.C. 103(a) as being unpatentable over Roth *et al.* and Son *et al.* is withdrawn.

As set forth previously, Applicants point out that the teaching of Son *et al.* no longer anticipates the embodiment of increasing efficiency at least 50% (page 8). Moreover, Applicants note that Son *et al.* try several anticancer agents, and besides cisplatinin none had any significant affect on transfection efficiency (pages 8-9). The teaching of Roth *et al.* fail to remedy the deficiencies of Son *et al.*, and provide no motivation to use the agents disclosed in Roth *et al.* (page 9 and paragraphs 8 and 11 of the declaration of Dr. MacLachlan). See Applicants' amendment, pages 8-9. Applicants' arguments have been fully considered, and found persuasive in part

Roth *et al.* was provided to teach the limitations of claims 52-54 which were canceled. The cancellation of the claims obviates the basis of the rejection.

Claims 38-44, 47-50, 69-73 and 78-86 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Roth *et al.*, Son *et al.* and Walker *et al.*

Applicants summarize arguments over Roth *et al.* and Son *et al.* and summarize the teaching of Walker *et al.* as a method for the delivery of a liposome composition and contains no mention for the use of the methodology in conjunction with a cell cycle blocker (page 9). Applicants argue that the teaching of Walker et al fail to cure the deficiencies of Sun et al. and Roth et al., and that Walker et al. provides no specific teaching to combine the methods of

providing a liposome with a cell cycle blocker to increase transfection efficiency as disclosed in Son *et al.* (page 10 and the declaration of Dr. MacLachlan). See Applicants' amendment, pages 9-10. Applicants' arguments have been fully considered, but not found persuasive.

The teaching of Walker *et al.* was provided to demonstrate that various methods for the delivery of liposomal compositions were known and practiced in the art. Examiner would agree that there was no specific motivation in Walker *et al.* to combine the methodology with a cell cycle blocker, however the methods of Walker *et al.* are general methods providing an improvement for the delivery of liposomal compositions. The successful results presented in Son *et al.* for the effectiveness of certain liposomal compositions provides motivation to use any delivery method conventional in the art. In particular the methods taught by Walker *et al.* provide an improvement for the increased efficiency of delivery of liposome compositions. The specific motivation of Son *et al.* to use their observation in gene therapy protocols provides adequate motivation to optimize known delivery protocols in maximizing the delivery of a given polynucleotide. Given the teachings and successful results of Roth *et al.* and Son *et al.* for the potential treatments of cancer cells, one would have been motivated to use the teachings of Walker *et al.* for delivery protocols who also discusses use of the delivery protocols as noted by Applicants for the killing of cells.

Therefore, for the reasons above and of record, the rejection is maintained.

Claims 74-77 and 87 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Roth *et al.*, Son *et al.* and Bally *et al.*

Applicants argue that combined the teachings of Roth *et al.* and Son *et al.* fail to meet the limitations of the present claims, and that Bally *et al.* fails to remedy the deficiencies. It is noted that Bally *et al.* dose not disclose the use of any cell cycle blocking agent and provides no motivation to combine the teachings with Roth *et al.* and Son *et al.* See Applicants' amendment, pages 10-11. Applicants' arguments have been fully considered, but not found persuasive.

As reasons with the teaching of Walker *et al.*, the teachings of Bally *et al.* was provided to demonstrate methods which were known and practiced in the art for the delivery of a polynucleotide. Examiner would agree that there was no specific motivation in Bally *et al.* to combine the methodology with a cell cycle blocker, however the methods of Bally *et al.* are general methods providing an improvement for the gene delivery methods. The successful results presented in Son *et al.* for the effectiveness of certain compositions provides motivation to use any delivery method conventional in the art. In particular the methods taught by Bally *et al.* provide an improvement for the increased efficiency of gene delivery. The specific motivation of Son *et al.* to use their observation in gene therapy protocols provides adequate motivation to optimize known delivery protocols in maximizing the delivery of a given polynucleotide. In light of the teachings and successful results of Roth *et al.* and Son *et al.* for the potential treatments of cancer cells, one would have been motivated to use the teachings of

Bally *et al.* for improved delivery protocols. Therefore, for the reasons above and of record, the rejection is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

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